AMENDMENTS

In the Abstract:

ABSTRACT OF THE DISCLOSURE

Bifunctional molecules and methods for their use in the production of binary or tripartite complexes in a host are provided. The bifunctional molecule is a conjugate of a drug moiety and a presenter protein ligand. The molecular weight of the bifunctional molecule is less than about 5000 daltons. In the subject methods, an effective amount of the bifunctional molecule is administered to the host. In certain embodiments, if the bifunctional molecule binds to the presenter protein a drug target to produce a tripartite complex, while in other embodiments the bifunctional molecule binds to either the presenter protein or the drug target, but not both, to produce a binary complex ~~that exhibits at least one of improved affinity, specificity or selectivity as compared to the corresponding free drug~~. The subject methods and compositions find use in a variety of therapeutic applications.

In the Claims:

Claims 1-22 (Cancelled).

23. (Currently Amended) A method for producing a tripartite complex in a mammalian host, said method comprising:

administering to said mammalian host an effective amount of a bifunctional molecule of less than about 5000 daltons consisting of a drug moiety ~~and~~ a linked to a ligand for a presenter protein endogenous to said mammalian host, wherein said drug moiety binds to a drug target and said ligand binds to a presenter protein that is not said drug target to produce said tripartite complex of said drug target, bifunctional molecule and presenter protein in said mammalian host.

24. (Original) The method according to Claim 23, wherein said tripartite complex is produced intracellularly.

25. (Original) The method according to Claim 23, wherein said tripartite complex is produced extracellularly.

26. (Original) The method according to Claim 23, wherein said drug target is a protein.

27. (Original) The method according to Claim 23, wherein said endogenous presenter protein is selected from the group consisting of: peptidyl-prolyl isomerases, Hsp90, steroid hormone receptors, cytoskeletal proteins, albumin and vitamin receptors.

28. (Original) The method according to Claim 23, wherein said bifunctional molecule is administered as a pharmaceutical preparation.

29. (Currently Amended) A method for producing an intracellular tripartite complex in a mammalian host, said method comprising:

administering to said mammalian host an effective amount of a bifunctional molecule of less than about 5000 daltons comprising a drug moiety ~~and a~~ linked to a endogenous presenter protein ligand, wherein the ~~target of~~ said drug moiety and the ~~target of~~ said endogenous presenter protein ligand are bind to different intracellular proteins to produce said intracellular tripartite complex;

~~so that said bifunctional molecule binds to said drug target and endogenous presenter protein to intracellularly produce said tripartite complex.~~

30. (Cancelled)

31. (Original) The method according to Claim 29, wherein said endogenous presenter protein is selected from the group consisting of: peptidyl prolyl isomerases, Hsp90, steroid hormone receptors and cytoskeletal proteins.

32. (Original) The method according to Claim 31, wherein said endogenous presenter protein is a peptidyl prolyl isomerase.

33. (Cancelled) A method for producing a binary complex in a host, said method comprising:

administering to said host an effective amount of a bifunctional molecule of less than about 5000 daltons comprising a drug moiety ~~and a~~ linked to a ligand for a presenter protein endogenous to said host, wherein said drug moiety binds to a drug target and said ligand binds to a presenter protein that is not said drug target;

to produce said binary complex comprising said bifunctional molecule and presenter protein.

34. (Cancelled) The method according to Claim 33, wherein said ligand for a presenter protein is a peptidyl prolyl isomerase.

35. (Currently Amended) A method for enhancing the selectivity of a drug for a target in a first cell as compared to a second cell, said method comprising:

contacting said first and second cells with a bifunctional molecule of less than about 5000 daltons comprising said drug and a linked to a ligand for a presenter protein present in said second cell but not in said first cell, wherein said drug binds to a drug target and said ligand binds to a presenter protein that is not said drug target;

to produce a binary complex comprising said bifunctional molecule and presenter protein in said second cell but not said first cell.

36. (Previously Presented) The method according to Claim 35, wherein said drug

is an antimicrobial agent.

37. (Original) The method according to Claim 35, wherein said ligand is a peptidyl prolyl isomerase ligand.

38. (Currently Amended) In a method of administering a drug to a host in need of said drug, the improvement comprising:

administering to said host an effective amount of a bifunctional molecule of less than about 5000 daltons consisting of said drug or a fragment thereof ~~and~~ a linked to a ligand for a presenter protein endogenous to said host, wherein said drug binds to a drug target and said ligand binds to a presenter protein that is not said drug target.

39. (Original) The method according to Claim 38, wherein said host is a mammalian host.

40. (Original) The method according to Claim 39, wherein said mammalian host is human.

41. (Original) The method according to Claim 38, wherein said drug is a small molecule.

42. (Original) The method according to Claim 38, wherein said drug binds to an extracellular target.

43. (Original) The method according to Claim 38, wherein said drug binds to an intracellular target.

44. (Original) The method according to Claim 43, wherein said presenter protein ligand is a peptidyl prolyl isom rase.

Claims 45 to 47 (Cancelled)

48. (Cancelled)

49. (Previously Presented) The method according to Claim 23, wherein said drug moiety and ligand of said bifunctional molecule are joined by a linking group.

50. (Previously Presented) The method according to Claim 29, wherein said drug moiety and ligand of said bifunctional molecule are joined by a linking group.

51. (Cancelled)

52. (Previously Presented) The method according to Claim 35, wherein said drug and ligand of said bifunctional molecule are joined by a linking group.

53. (Previously Presented) The method according to Claim 38, wherein said drug and ligand of said bifunctional molecule are joined by a linking group.